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Stamler

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(54) **METHODS FOR PRODUCING AND USING S-NITROSOHEMOGLOBINS**

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(58) **Field of Search** 514/2, 6, 832; 530/385, 829; 604/28, 52

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(57) **ABSTRACT**

Nitric oxide (NO) interacts with hemoglobin (Hb) at its metal centers, whereas S-nitrosothiols (RSNOs) can donate the NO group to β93 cysteine residues, thereby shielding the NO functionality from heme inactivation. S-nitrosylation of Hb is under the allosteric control of oxygen and the oxidation state of heme. NO group release from S-nitrosohemoglobin (SNO-Hb) is further facilitated by intracellular low molecular weight thiols, forming RSNOs which can be exported from the erythrocyte to regulate blood pressure. Hence, a dynamic cycle is established in which S-nitrosylation of Hb is initiated in the lung following oxygenation of red blood cells and is completed by SNO-Hb metabolism during arterial-venous transit. SNO-Hb can be formed by reaction of Hb with S-nitrosothiol. This procedure avoids oxidation of the heme. SNO-Hb in its various forms and combinations thereof (oxy, deoxy, met; S-nitrosylated to various extents) can be administered to a mammal in a method of therapy where it is desired to oxygenate, to scavenge free radicals, or to release NO groups to tissues. Thiols can also be administered to enhance the transfer of NO groups. Examples of conditions to be treated by SNO-Hb therapy include ischaemic injury, hypertension, angina, reperfusion injury and inflammations.

5 Claims, 6 Drawing Sheets